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UPDATE ARTICLE

Management Of Heart Failure With Current Perspectives

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Introduction

Heart failure is defined as a pathophysiological state in which an abnormality of cardiac function is responsible for the failure of the heart to pump blood at a rate commensurate with the requirements of the metabolising tissues and/or to be able to do so only from an elevated filling pressure.¹ This abnormality in cardiac function is reflected by the occurrence of exercise intolerance. Although heart failure is known for a long time in medical history, this condition is still associated with high morbidity and mortality. Various studies have demonstrated around 50% mortality rate over 2-5 years or an annual mortality rate of about 25% in patients with left ventricular dysfunction.^{2,3} In addition, repeated hospitalisation for treatment of worsening heart failure has placed a severe strain on the health care system. In this article, the preventive and treatment strategies currently available for the management of heart failure will be discussed.

Keywords: Heart failure, aetiology, diagnosis, management

Aetiology

In North America, between 60-70% of adult patients with heart failure have left ventricular

dysfunction secondary to ischaemic heart disease, and nonischaemic dilated cardiomyopathy accounts for approximately 20% of patients with heart failure.⁴ In Hong Kong, coronary artery disease is now the most common cause of heart failure. This is due to the increasing incidence of coronary artery disease as society becomes more westernized, the increasing proportion of the elderly in the population and improved survival in patients with established heart failure and myocardial infarction. Hypertensive cardiovascular disease is probably the second most common cause. On the other hand, congestive heart failure (especially refractory right heart failure) resulting from rheumatic valvular problems still remains an important disease. Idiopathic dilated cardiomyopathy, post-viral myocarditic cardiomyopathy, undiagnosed / inoperable congenital heart disease, untreated chronic tachyarrhythmia are some of remaining causes for patients hospitalised for heart failure.

Pathophysiology of Heart Failure

Heart failure is associated with changes involving the heart as well as the peripheral circulatory system (**Figure 1**). The initial insult is usually an abnormal increase in after-load or significant loss of functioning myocardium. Development of myocellular hypertrophy and alterations in collagen matrix occur which ultimately results in geometric changes (remodelling) of the left ventricle and reduced cardiac output. During this process, baroreflex responses are attenuated and a variety of neurohormonal systems are activated. Some of the vasoconstrictor neurohormone systems, i.e. the sympathetic nervous system, angiotensin II, aldosterone and endothelin, may also act directly on

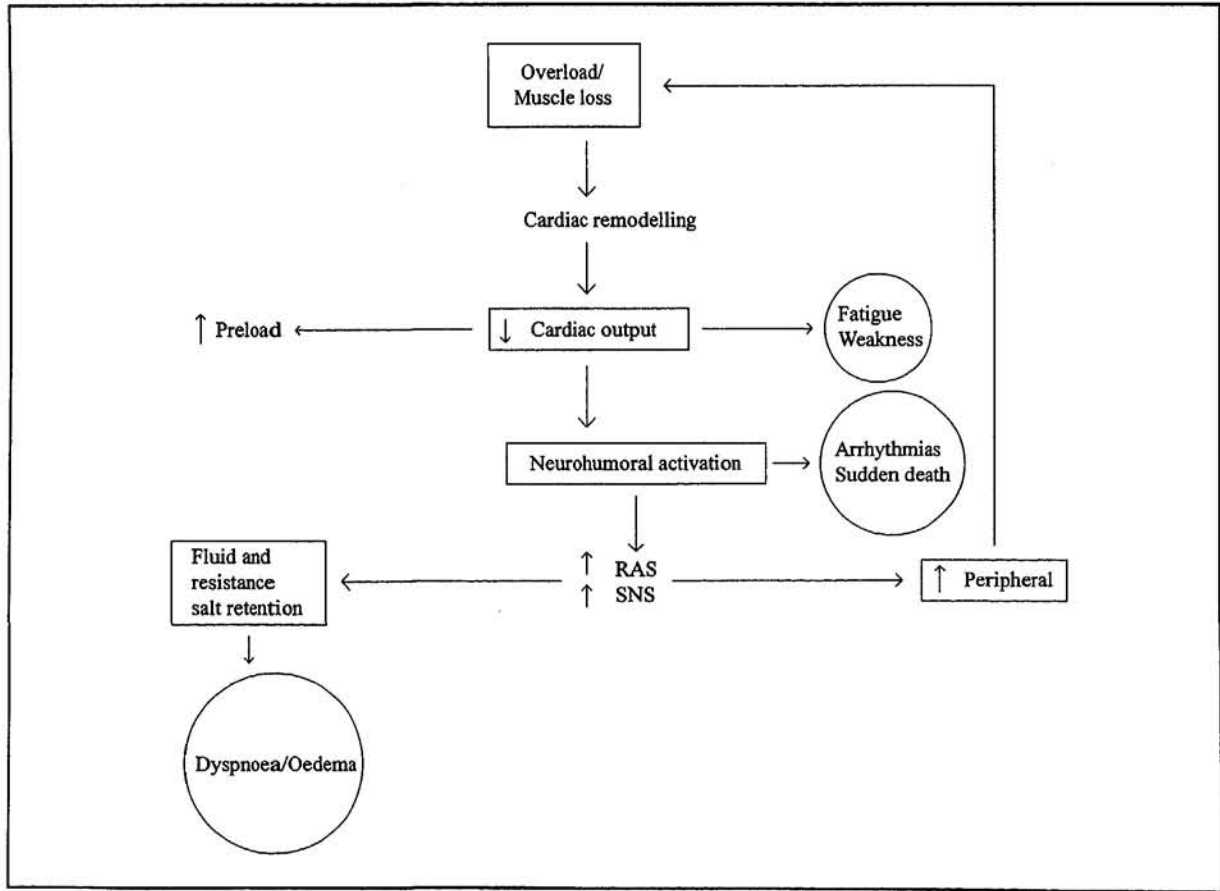
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the heart by further increasing cellular hypertrophy, collagen synthesis and promoting increased cytosolic calcium. These actions create a cycle within the heart resulting in increased myocardial energy expenditure, hastening cell injury and induction of lethal arrhythmias. These neurohormones also induce systemic arterial and venous vasoconstriction, vascular remodelling and endothelial dysfunction. These effects increase the afterload to the heart and promote salt and water retention in the kidney, leading to circulatory congestion. Altered blood flow to the skeletal muscle and diminished baroreceptor

response to stress and pulmonary congestion further contribute to decreased exercise performance.⁵⁻⁷ The overall effects will be clinically manifested by an elevation in left ventricular end-diastolic pressure, low cardiac output state, peripheral oedema and dyspnoea, and these adaptive cardiac and non-cardiac changes further worsen heart failure. Although other neurohormones such as the natriuretic peptides and some prostaglandins are vasodilatory and natriuretic, the extent of the modulation is usually not sufficient to break the aforementioned vicious cycles, especially in the advanced stage of the disease.

Figure 1: The Pathophysiology of heart failure involves the Interaction of Intrinsic Cardiac Function with Neurohormonal Activation, Peripheral Vasoconstriction and Volume expansion. Clinical Effects are Encircled.



RAS = Renin Angiotensin System, SNS = Sympathetic Nervous System

Systolic / Diastolic Dysfunction

The majority of patients with chronic heart failure will have elements of both systolic and diastolic dysfunction. The hallmark of systolic dysfunction is a reduced cardiac ejection fraction due to myocardial injury or cell death. Systolic dysfunction is likely to be the predominant problem in patients with previous myocardial infarction or idiopathic dilated cardiomyopathy. Diastolic dysfunction reflects changes during the diastolic period and includes alterations in myocardial relaxation (reflected by changes in early diastole), and ventricular compliance (reflected by changes later in diastole). Since diastolic relaxation is not a passive process but requires energy, diastolic dysfunction may result from any condition where myocardial demands exceed supply e.g. myocardial ischaemia. Ventricular interdependence and pericardial restraint will also influence diastolic function as in cases of restrictive cardiomyopathy and constrictive pericarditis.⁸

Most of the recent large mortality trials in heart failure have enrolled patients with predominant systolic dysfunction, providing new insights for their management. However, the definitive treatment of patients with diastolic dysfunction remains controversial. On the other hand, increased left ventricular mass and hypertrophy are still important determinants of impaired ventricular filling, a decrease in left ventricular wall thickness and mass appears to be a rational objective of treatment of diastolic ventricular failure. Angiotensin converting enzyme inhibitors, calcium channel blocking agents, beta-adrenergic blocking drugs and centrally acting sympatholytic agents have been shown to be potentially effective in reducing left ventricular mass. However, in patients with overt heart failure, diuretic therapy will be needed,⁹ but excessive diuresis may be detrimental as left ventricular filling is now dependent on a higher than normal filling pressure.

Clinical Findings in Heart Failure

In severe heart failure, symptoms will usually be obvious and generally include fatigue, dyspnoea, peripheral oedema, orthopnoea, paroxysmal nocturnal dyspnoea, cough, weight gain, abdominal discomfort, and cool extremities. Patients with less severe heart failure may be asymptomatic at rest and have only modest limitation in activities. The New York Heart Association (NYHA) classification is widely used to grade the degree of symptoms of adult heart failure patients (Table 1).

Table 1: New York Heart Association Classification of Heart Failure

Class I	No symptoms
Class II	Symptoms with ordinary activity
Class III	Symptoms with less than ordinary activity
Class IV	Symptoms at rest

Nevertheless, symptoms might not always correlate with severity of left ventricular dysfunction. Sometimes, patients with severe left ventricular systolic dysfunction still remain relatively asymptomatic; and bear in mind the fact that prognosis of patients with heart failure depends very much on residual left ventricular function (ejection fraction) rather than heart failure symptoms.

On physical examination in patients with severe heart failure, a low or normal blood pressure may be found. Sinus tachycardia (heart rate above 100 beats/min) is common, and pulsus alternans may be present. The periphery may be characteristically cool with oedema of varying degrees. Patients may be diaphoretic and appear cyanotic. The lung signs include tachypnoea, crackles, wheezing and pleural effusion. Palpation of the cardiac apex usually reveals a displaced apex laterally. Tachycardia, gallop rhythms (S₃ and S₄) and murmurs of mitral regurgitation are very common. In severe cases of right sided failure,

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tricuspid regurgitation is present, the jugular venous pressure is elevated and hepatojugular reflex is positive. Hepatosplenomegaly, and occasionally ascites, may be observed.

Chest radiography will characteristically show cardiomegaly, the presence of interstitial oedema, vascular redistribution, peribronchial cuffing and pleural effusions. Calcification of the aortic or mitral valves may be present, as well as calcification in a left ventricular aneurysm.

ECG findings vary considerably. Atrial fibrillation and atrial flutter are common as are supraventricular and ventricular ectopic beats. Nonspecific ST-T wave changes may occur, and it is not uncommon to find evidence of an old myocardial infarction or left ventricular hypertrophy. Prior Q wave myocardial infarction (Figure 2), particularly in two different regions, suggest systolic dysfunction, while left ventricular hypertrophy may be associated with diastolic dysfunction. A complete left bundle branch block may represent an underlying cardiomyopathy or may obscure underlying Q waves from prior myocardial infarction.

Complete blood count is useful to exclude anaemia. A haemoglobin below 9 g/dL may precipitate or aggravate congestive heart failure.

Serum sodium is an excellent and inexpensive test that indicates neurohormonal activation. Sodium level is also inversely proportional to plasma renin level¹⁰ and the lower the sodium, the higher the renin and the worse the prognosis for survival. Serum potassium is also important. Maintenance of a potassium level on the high side e.g. 4.0 to 5.0 mmol/L is recommended, as the serum potassium underestimates intracellular potassium level. The lower the potassium, the worse the prognosis, and the same holds true for magnesium.¹¹ Renal function is often abnormal in patients with severe heart failure. Both urea and creatinine may continue to increase with deteriorating left ventricular function and the need for high dose diuretic therapy. Serum electrolytes and uric acid are frequently altered by diuretic therapy. Severe right-sided heart failure may impair liver function. A thyroid function test is important to exclude thyroid dysfunction as a cause of heart failure (Table 2).

Figure 2: Patient with Old Extensive Anterior Myocardial Infarction and Left Ventricular Aneurysmal Dilatation

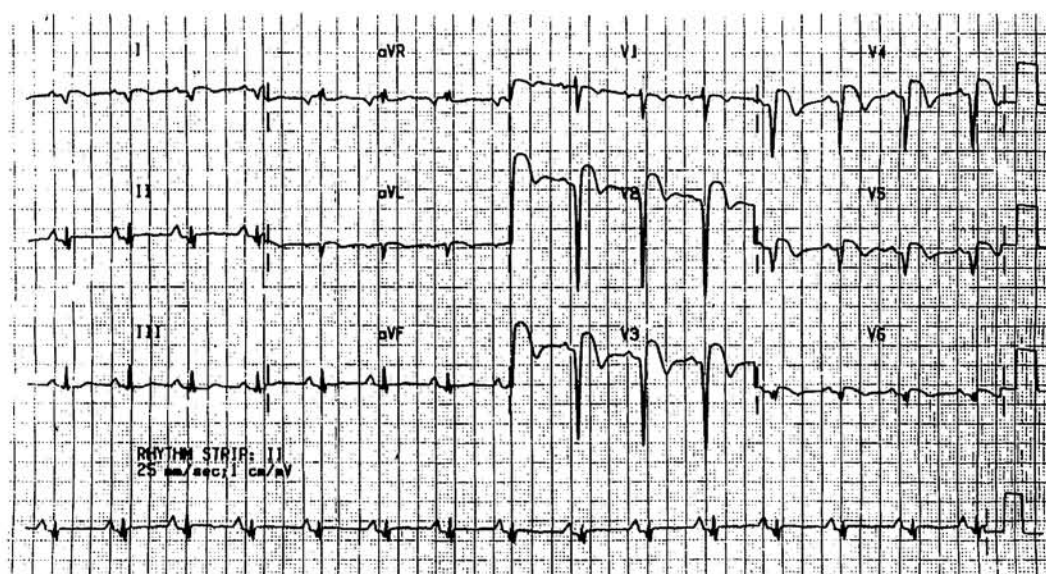


Table 2: Diagnostic and Evaluation Investigations

Laboratory Tests:	Complete Blood Picture RFT, LFT, urate Thyroid Function Test
Non-invasive Tests:	CXR, ECG Echocardiography Exercise Testing Radionuclide Imaging
Invasive Tests:	Haemodynamic Monitoring Cardiac Catheterisation +/- Biopsy

Cardiac Diagnostic Tests

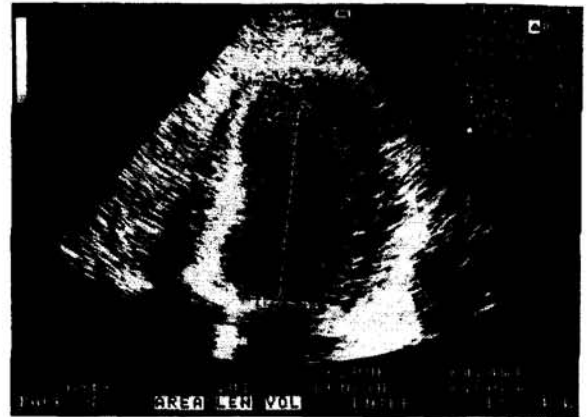
Non-Invasive

Objective noninvasive assessments of cardiac performance are indicated in all patients with known or suspected heart failure. The data obtained by these techniques help to differentiate systolic from diastolic dysfunction, exclude other causes of dyspnoea such as pulmonary diseases and are predictive of outcome and may guide the selection of therapy in individual patients. Each technique provides different kinds of information, and depending on the specific information sought, one or the other test may be performed.

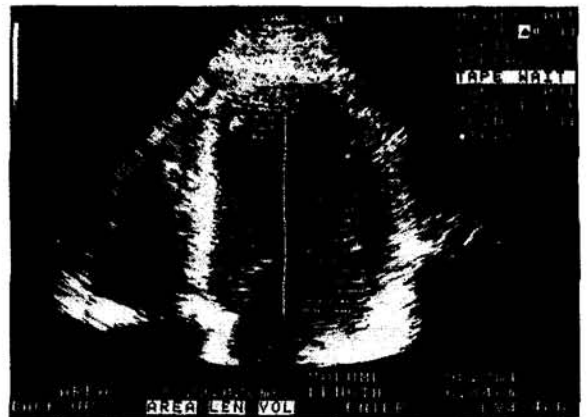
Echocardiography is imperative in patients with heart failure to provide a low cost, comprehensive, noninvasive diagnostic and prognostic assessment with measurement of ventricular function, chamber dimension, muscle mass, valvular function, detection of intracardiac thrombus or masses, and indirect estimation of cardiac haemodynamics¹² (Figure 3).

Figure 3: Two-dimensional Echocardiography in a Patient with Dilated Cardiomyopathy (Ejection Fraction = 35%)

(a) Systole



(b) Diastole



Radionuclide angiography is recommended in patients with heart failure as an accurate, reproducible noninvasive technique for measurement of ventricular function and left ventricular ejection fraction.¹³ The myocardial stress thallium imaging (either induced by exercise or by pharmacological means) is frequently employed to look for reversible myocardial ischaemia in patients with heart failure. This imaging technique may be particularly useful when revascularisation procedures are being considered in heart failure patients.¹⁴

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An exercise test, especially coupled with cardiopulmonary assessment, may be used to exclude irreversible causes of heart failure. In addition, this also helps to confirm a diagnosis of limited functional capacity, to assess major limiting symptoms, to monitor response to therapy or to prescribe appropriate level of daily activities.

Invasive

In critically ill patients, clinical assessment of the severity of the haemodynamic abnormalities is frequently inaccurate and haemodynamic monitoring may confirm the mechanism and the severity of the low output state. However, haemodynamic monitoring is usually not required for the initiation of therapy with vasoactive drugs in patients with stable chronic heart failure.¹⁶

Coronary angiography is not routinely required in patients with congestive heart failure. Most patients in whom left ventricular dysfunction are secondary to coronary artery disease have had a previous myocardial infarction and, therefore, the primary diagnosis of their condition is usually not in doubt. Patients who present with anginal symptoms despite medical therapy or documented evidence of myocardial ischaemia should undergo a complete evaluation including coronary angiography, and an indication for myocardial revascularisation should be determined. In some cases, the aetiology of the cardiomyopathy may be uncertain, and this must be established by coronary angiography.

At present, routine endomyocardial biopsies are not recommended in patients with dilated cardiomyopathy since the likelihood of making diagnoses of treatable disease is too low to justify the small risk of cardiac perforation. In addition, endomyocardial biopsies are not indicated in patients with suspected myocarditis because the frequency of diagnostic biopsies is low and there are no convincing data to support the use of immunosuppressive therapy. However, endomyocardial biopsies are recommended for the diagnosis of cardiac lesions in

which there are known therapies, and when the diagnosis cannot be made reliably without a cardiac biopsy e.g. diagnosis of cardiac allograft rejection.¹⁷ The prognostic indicators of heart failure are summarized in Table 3. The functional state of the patients and exercise capacity are excellent indicators of survival.

Table 3: Prognostic Indicators of Survival in Heart Failure

• Functional Class
• Exercise Capacity and Maximum Oxygen Consumption
• Presence of Residual Ischaemia
• Serum Sodium
• Serum Catecholamines
• Ejection Fraction

Medical Treatment of Heart Failure

General

The goals of treatment of heart failure are to reduce symptoms, decrease the need for repeated hospitalisations and improve survival. In addition, the factors which precipitate or aggravate heart failure should be recognised and managed in concert with the heart failure. The role of a Cardiac Rehabilitation Programme is well recognised, and has been documented to reduce reinfarction and exercise performance in patients with heart failure. In short, it is a programme that concentrates various faculties such as doctors, nursing staff and allied health professionals to give a more efficient services. The aims of the program include: firstly, risk factors modification in patients with established coronary artery disease; secondly, education and counselling of patients and family members on the understanding of disease and finally, the advisability of light regular activity commensurate with patients' functional capacity. Structured exercise programmes improve exercise capacity and decrease symptoms, although the long term efficacy in survival remains to be studied.

Diuretics

Diuretics remain useful for management of heart failure.¹⁸ The principal mechanism of action is to reduce excessive salt and water retention with a reduction in preload, which results in a decrease in symptoms from pulmonary and systemic congestion. Most symptomatic patients will require diuretic therapy, may be in low doses, and combination diuretic therapy is helpful in refractory heart failure. It is conventional to use a potassium sparing agents before stepping up high dose loop diuretic. Furthermore, such combination diuretic therapy may ensure a more efficient diuresis since they act on different sites of the renal tubular system. Nevertheless, major adverse effects include excessive reduction in preload with reduced cardiac output, aggravation of fatigue, electrolyte disturbances, prerenal renal failure and neurohormonal activation may be harmful in patients. The possibility of inducing hyperkalaemia and further renal dysfunction when using combination diuretic therapy together with the almost ubiquitous use of angiotensin converting enzyme (ACE) inhibitor should be considered. The optimal dose of diuretic is determined by minimal oedema and congestion without compromising the cardiac filling pressure. This is determined by a jugular venous pressure of <8 cm of water and absence of significant hepatojugular reflex and prerenal azotaemia (Table 4). Patients should keep daily charts of their optimal body weight and serum electrolytes should be closely monitored.

Table 4: Diuretics – Practice Points

- Thiazide diuretics not useful if creatinine clearance <30 ml/min
- Frusemide should be started at 20-40 mg/day. Single dose up to 160 mg/day more effective than divided doses
- Aviod NSAID
- Monitor potassium level twice weekly until stable (aim at ≥ 4 mmol/l)
- Monitor daily body weight (optimum wt: JVP <8 cm, no HJ reflex)

ACE Inhibitors

ACE inhibitor therapy has been shown to reduce mortality, improve quality of life (decrease hospitalisation, increase exercise tolerance) and reduce the risk of myocardial infarction in patients with NYHA class II to IV congestive heart failure.¹⁹

²¹ Patients with the lowest ejection fractions and worst symptoms derive the most benefit. In asymptomatic patients with left ventricular dysfunction, ACE inhibitors can also prevent deterioration to overt heart failure and prevent myocardial infarction in patients with LVEF 35% or less.²² In the early post infarct period²²⁻²⁶, as well as in the days after, starting ACE inhibitors have been shown to decrease mortality, prevent progression to overt heart failure and to reduce the risk of recurrent myocardial infarction.²⁷⁻²⁹ The improvement in both short-term and long-term outcome suggests that the benefit of ACE inhibitors may not be due entirely to an attenuation of ventricular remodelling, which could be expected to occur over a long period, thus it is postulated that most of the benefit is achieved through a primary cardioprotective effect as well as through the prompt blockade of the deleterious effects of neurohumoral activation.³⁰⁻³¹ Side effects of ACE inhibitors include cough, hypotension (especially first-dose effect), angioedema, altered taste sensation, skin rash and rarely, reversible bone marrow suppression. Patients at greatest risk of worsening renal function and hyperkalaemia include those with bilateral renal artery stenosis, renal impairment and hypertension. Though ACE inhibitors has been shown to differ in affinity for receptors in cardiac and peripheral tissues, these significance requires further evaluation and their preferred use in particular clinical situations e.g hypertension need further study;³²⁻³³ but the consensus still hold that ACE inhibitors appear largely interchangeable, the efficacy seem to be a class effect rather than the action of a particular prototype. Similarly, the issue on which dosage of ACE inhibitor should be used clinically remain disputed and certainly await further studies (such as the latest ATLAS trial which assess the efficacy of different doses of ACE inhibitors in the management of heart failure). However, the

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appropriate doses used in these large mortality trials can be used as initial guidelines. Practical points for the usage of ACE inhibitors are listed in Table 5.

Table 5: ACE Inhibitors – Practice Points

- Exclude volume depletion:
orthostatic hypotension, prerenal azotaemia, metabolic alkalosis
- First dose hypotension and elderly:
test dose e.g. 6.25 mg captopril (or 2.5 mg enalapril) then 12.5 mg tds
- Monitor weekly for:
increase in serum creatinine ($>40 \mu\text{mol/l}$)
potassium level $> 5.5 \text{ mmol}$
symptomatic hypotension
- Efficacy may occur only after several months
- Consider hydralazine/isosorbide if ACE Inhibitors not tolerated
- Dose: captopril 2.5 mg tds to 50 mg bd
enalapril 2.5 mg Qd to 10 mg bd
If serum creatinine $>250 \mu\text{mol/l}$ — half dose
- Cough: may be due to worsening heart failure
reduce dose and reassurance, try anti-tussive
- Avoid potassium-sparing diuretics

Other Vasodilators

Losartan, an orally active, non-peptide angiotensin II receptor antagonist has been introduced to provide pharmacological blockade of the renin-angiotensin-aldosterone system. Its effect on blood pressure, renal function, systemic and regional haemodynamic effects seems comparable to ACE inhibitors.³⁴ The main advantages of Losartan over ACE inhibitors are firstly, the adverse effects seen with ACE inhibitors that are attributed to non-renin angiotensin system effects (notably angioedema and cough) may be less frequent in patients treated with a selective angiotensin II receptor blocker. Secondly,

enzymes have been described which are capable of producing angiotensin II via metabolic pathways independent of the classical renin-angiotensin system route, thus bypassing the action of ACE inhibitors. Losartan, being an angiotensin II receptor blocker, can antagonise the effects of the end-product (angiotensin II) specifically.³⁵⁻³⁷ In clinical studies, there are supporting evidence that short-term administration of Losartan in patients with symptomatic heart failure has resulted in beneficial haemodynamic effects.³⁸ Though its long term benefits especially on importance in survival awaits further studies for documentation. Nevertheless, Losartan may be an alternative to patients who cannot tolerate ACE inhibitors because of their side effects.

Hydralazine and nitrates in combination improve exercise tolerance and appear to improve survival in patients with NYHA class II to III heart failure³⁹, though this drug combination is not well tolerated in as most as one-third of patients. Furthermore, the improvement in survival appears to be less than with ACE inhibitors.⁴⁰ Therefore, they may be used as an alternative for patients who are intolerance of ACE inhibitors. Whether these could be used in combination with ACE inhibitors remain uncertain.

First-generation calcium channel blockers (nifedipine, diltiazem, verapamil) are not recommended for routine use in patients with systolic dysfunction;⁴¹⁻⁴² newer agents (amlodipine, felodipine and nicardipine) are being assessed in ongoing clinical trials but are also not recommended for routine use in heart failure.⁴³⁻⁴⁴ There is no data concerning the role of other vasodilators such as prazosin, minoxidil and alpha-methyl-dopa.

Digitalis and Other Inotropic Drugs

The use of positive inotropic agents in patients with heart failure has been the subject of great controversy. The variety of agents that have been proposed are generally classified as digitalis glycosides or nonglycosides, and the latter includes

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phosphodiesterase inhibitors, beta-adrenergic receptor agonists and dopaminergic-receptor agonists. In view of their haemodynamic profile, the phosphodiesterase inhibitors initially appeared to be a welcome addition to therapies for heart failure, but subsequent clinical trials with drugs such as milrinone and enoximone indicated that these agents were not only of no benefit, but had an adverse effect on survival.⁴⁵⁻⁴⁶ These drugs continue to be used intravenously to treat acute haemodynamic situations but they have no role in the long term management of heart failure.

The parent dopaminergic agents, dobutamine and dopamine, are only of limited value in the long term management of heart failure, primarily because of their mandatory intravenous route of administration. Intermittent administration, either as in out-patient or during brief hospital admission, has resulted in haemodynamic improvement, questionable improvement of symptoms and no improvement on survival.⁴⁷⁻⁴⁸ Ideally, dobutamine should be administered initially in a hospital intensive care unit setting and a dose-response curve constructed using haemodynamic monitoring. The usual starting dose is 2.5 $\mu\text{g/kg/min}$ and the dose titrated to optimise cardiac index. Although up to 15 $\mu\text{g/kg/min}$ may occasionally be acutely used, 80% of the maximum haemodynamic response is generally observed at 6 to 8 $\mu\text{g/kg/min}$ – the usual dose used for home intravenous therapy. A recent study suggested that by avoiding a high dose, dobutamine appears to be well tolerated and may significantly improve symptoms.⁴⁹

In patients with atrial fibrillation and left ventricular failure, digoxin should be the initial agent used for this clinical situation because both beta-blockers and/or calcium channel antagonists may have negative inotropic effects and therefore be relatively contraindicated. However, the inability of digoxin to control exercise-induced tachycardia adequately in this clinical setting often requires the addition of one of these agents. In patients with sinus rhythm, a large body of evidence indicates indirectly that digoxin is useful in improving

symptoms, increasing exercise tolerance, improving the ejection fraction, and will result in clinical deterioration when discontinued;⁵⁰⁻⁵³ one of which was the RADIANCE Trial, which studied patients with NYHA functional class II or III heart failure and an ejection fraction <35% who were clinically stable while receiving digoxin, diuretics and an ACE inhibitor. Patients were randomised to either continue digoxin therapy or receive placebo for 12 weeks. Digoxin withdrawal was associated with significant clinical deterioration, including reduction in exercise time, an increased need for emergency care/ hospitalisation for decompensated heart failure and a lower quality of life score. Nevertheless, the issue of whether digoxin prolongs life in patients with heart failure remains to be answered, but is the prime outcome being tested in the ongoing Digoxin Investigation Group (DIG) mortality trial in 1995 (Table 6).

Table 6: Digoxin – Practice Points

- Indicated in more severe HF:
EF <40 %
Symptomatic after ACE Inhibitors
- No loading dose:
Normal RFT: 0.25 mg/day and level in 1 week
Abnormal RFT: 0.125 mg/day and level in 2-3 weeks
- Digoxin toxicity:
Confusion, nausea, anorexia, visual change, arrhythmias
- Digoxin interaction:
Quinidine, verapamil, amiodarone, antibiotics, anticholinergics

The recent observation that vesnarinone, a new non-phosphodiesterase inhibitor inotropic agent, reduces morbidity and mortality in patients with heart failure requires supporting confirmation studies before its routine use can be recommended.⁵⁴ Its mechanism of action is not fully understood but postulated to serve as an immunomodulator by inhibiting cytokines production stimulated by the failing heart.⁵⁵⁻⁵⁶

Beta-blockers

Beta-blockers have been postulated in positively modifying the pathophysiological pathways of mortality and morbidity in heart failure by reducing neuroendocrine activation, reduction in myocardial ischaemia and suppression of ventricular arrhythmias. Nevertheless, there has been a widespread reluctance to use beta-blockers in heart failure for fear of worsening the congestive heart failure. Certainly, beta-blockers is indicated in the management of post-myocardial infarct patients.⁵⁷⁻⁵⁹ In addition, the impact of beta-blocker in patients with idiopathic dilated cardiomyopathy has been addressed in one large randomised trial which showed reduction in deaths or the need of heart transplantation as well as less clinical deterioration in heart failure parameters.⁶⁰

One of the problems of beta-blocker is the non-selective beta-2-blocking effects on the arterial tree, resulting in vasoconstriction and compromisation of tissue flow. Therefore, beta-blocker with partial agonistic action may offer a benefit over conventional ones. In a randomised study performed by our institution on the use of labetalol⁶¹ which possess alpha-agonist property, there is an increase in exercise performance compare with placebo. A new third generation beta-blockade (e.g. Carvediol) has been developed with combined vasodilatory and alpha-blockade effects.⁶²⁻⁶³ Its advantages in minimising myocardial depression and at the same time preventing natural progression of heart failure draw a lot of enthusiasm. Several small studies have shown improvements in ejection fraction and reduced left ventricular dimensions with its use, and in preliminary reports a survival benefit was observed for all classes of heart failure with the use of carvediol when compared with placebo⁶⁴.

Treatment of Refractory Heart Failure

Patients who remain symptomatic with signs of severe heart failure despite standard therapy for heart failure represent a serious medical condition with a

very poor prognosis, as many as 50% of these patients dying within three to six months. Clearly, the best option is cardiac transplantation. However, due to the limited capacity of this option, other strategies have been developed. General supportive measures form the cornerstone of therapy. These include salt and fluid restriction, a balanced diet and rest periods, particularly after meals. The use of various combination of diuretics has proven useful in improving some patients with refractory heart failure. Combination diuretics, such as frusemide, thiazides, metolazone, triamterene or spirono-lactone can be very useful. However, the risks of combination diuretics are not negligible, and include hyper- or hypokalaemia, hyponatremia and worsening renal failure. Some reliable patients can regulate their daily dosage of diuretics according to daily weights taken at home. Combination of various vasodilators can also be useful. In addition to ACE inhibitors, nitrates and hydralazine can be added to the regimen but careful monitoring of blood pressure is required and in some patients, haemodynamic monitoring is needed to balance optimal therapy against the hypotensive effects of the agent. During periods of acute decompensation, intravenous nitroglycerine (1 to 2 $\mu\text{g/kg/min}$) and dobutamine/ dopamine have been found to be useful in some patients. However, patients should be monitored closely for arrhythmias, electrolyte imbalances and haemodynamic disturbances. Finally, short-term use of nitroprusside and amrinone infusions can also be considered as last resorts (Table 7).

Table 7: Persistent Heart Failure

- Exclude reversible causes:
e.g. compliance, dietary indiscretion, anaemia, infection, NSAID
- Diuretics
Large dose (e.g. frusemide 480 mg/day)
Intravenous diuretics
Metolazone 2.5 mg single dose
- Spironolactone (beware of hyperkalaemia)
- Hydralazine/isosorbide
PND: nitrate patch at sleep
- Transplantation

Surgical Treatment for Heart Failure

Coronary artery disease is a major cause of heart failure. Although the risk of revascularisation is increased in patients with poor left ventricular function and severe coronary artery disease, long term surgical survival benefits appear greatest in patients with the most severe left ventricular function, coronary disease and anginal symptoms. Therefore, patients with coronary artery disease and demonstrable ischaemia should be considered for revascularisation. A low ejection fraction or presence of congestive heart failure should be an indication rather than a contraindication to surgery.⁶⁵⁻⁶⁸

In patients with potentially resectable left ventricular aneurysm, aneurysm resection with or without bypass grafting should be considered, and in patients with overt heart failure it is recommended surgery should be performed before severe irreversible global dysfunction or acute decompensation occurs.⁶⁹ In addition, patients with life threatening ventricular arrhythmias and coronary artery disease with an area of resectable scar should be referred for consideration of map-directed surgical resection and cure of their ventricular tachycardia at the time of revascularisation and left ventricular repair.⁷⁰ Lastly, the importance of valvular repair or replacement in the treatment of heart failure should be remembered.

Cardiomyoplasty is an experimental technique that may be of benefit in selected groups of patients with severe congestive heart failure and dilated cardiomyopathy as a bridge to cardiac transplantation. In addition, small studies have shown improvements in functional class and short term survival with this surgical technique.⁷¹⁻⁷²

Other forms of ventricular assist devices (e.g. Heart Mate) and the total artificial heart

are still under clinical trial and the routine use in clinical practice require further supporting data.⁷³⁻⁷⁴ At present, these are still bridging devices to maintain the life of patients prior to cardiac transplantation.

Cardiac Transplantation

The most common indications for heart transplantation in adults are cardiomyopathy and coronary artery disease. Outcome has improved with the introduction of the immunosuppressant cyclosporine in the early 1980s. Five-year survival after transplantation now exceeds 70%, one-year survival is around 88% and the 30-day mortality is 10% due to graft failure, acute rejection or infection.⁷⁵ However, after two years, accelerated coronary artery disease, probably on an immune basis, becomes the leading cause of death; and these patients may die suddenly as they do not experience angina because of surgical denervation. In addition, the accelerated atherosclerosis differs from the usual variety in that it is more diffuse, distal, cellular, with less lipid accumulation and collateral vessels are rare.⁷⁶⁻⁷⁷

Principal selection criteria for candidates suitable for heart transplantation are intractable heart failure despite optimal medical therapy and not amenable to conventional surgery, with a poor 12-month prognosis and with likelihood of rehabilitation. Contraindications to heart transplantation include recent malignancy, recent drug or alcohol abuse, untreated infection, irreversible renal disease (creatinine greater than 200 $\mu\text{mol/L}$) or hepatic disease, irreversible pulmonary hypertension (pulmonary vascular resistance more than 6 Wood units), surgical technical factors, noncompliance with medical care, poor rehabilitation potential, severe peripheral or cerebrovascular disease, marked cachexia or obesity, and insulin-dependent diabetes with end organ disease. With

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experience, the number of absolute contraindications to heart transplantation have declined.⁷⁸⁻⁷⁹

Ancillary Treatment

Anticoagulant therapy is strongly recommended in all patients with heart failure and associated atrial fibrillation. However, in patients who are noncompliance or at risk from warfarin therapy, aspirin is recommended. Although anticoagulation is not recommended as a routine in heart failure patients with sinus rhythm, it should be considered in patients with severe LV dysfunction, demonstrated intracardiac thrombus, or other risks for arterial or venous thrombosis.⁸⁰ However, a recent meta-analysis showed that patients with severe heart failure in sinus rhythm gain no benefit from anticoagulation.⁸¹ Thus, in an uncomplicated patient with heart failure, the routine of anticoagulation, with its inherited risk and the need for monitoring, is not recommended.

Antiarrhythmic therapy is indicated for patients with severe symptomatic rhythm disturbances. Patients with near miss sudden death, ventricular fibrillation and sustained ventricular tachycardia require effective therapy. Atrial arrhythmias, particularly atrial fibrillation, can result in significant disability. The use of antiarrhythmic drugs, however, is not only generally less effective and associated with increased risk of proarrhythmic effects in the setting of heart failure, but are also associated to a varying degree with negative inotropic effects, making control of heart failure more difficult. Drug therapy is recommended only for life-threatening or significantly symptomatic arrhythmias. Type I agents (quinidine, procainamide, disopyramide, flecainide, propafenone) should be avoided. Type III drugs such as sotalol and amiodarone are effective and usually considered first-line agents.⁸² Recently, the Grupo de Estudio de la Sobrevida en la

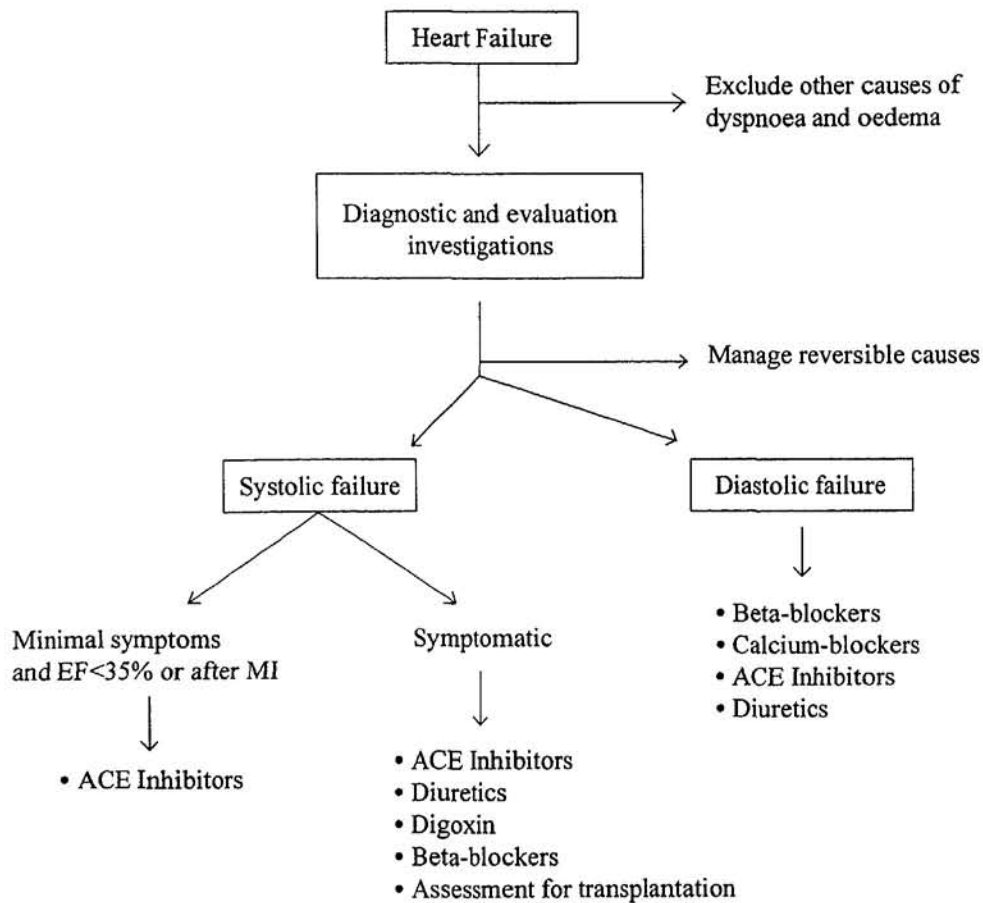
insuficiencia Cardiaca en Argentina (GESICA) trial suggested that low dose amiodarone can decrease mortality (both sudden death and death due to progressive heart failure) and hospital admission in patients with heart failure in a population that was mainly represented by dilated cardiomyopathy.⁸³⁻⁸⁴

Patients with severe heart failure have a significant risk of sudden cardiac death which may be unpredictable and the routine use of an implantable cardioverters/defibrillators (AICD) in such patients is a matter of intensive clinical research. At present, it is implanted in patients, as a form of life-saving device, who are prone to develop haemodynamically unstable ventricular tachyarrhythmia (as an alternative to anti-arrhythmic therapy) for the prevention of sudden cardiac death. With the use of tranvenous AICD and lower risk of their implantations, a wider use of such devices are expected.

Summary

All patients with known or suspected heart failure should undergo a detailed history and physical examination. Other causes for the symptoms and/or clinical signs indicative of heart failure should be excluded. Routine biochemical tests, as well as a standard chest x-ray and ECG, should be performed on all patients with heart failure. Precipitating or aggravating causes of heart failure should be eliminated. Patients with potentially surgically correctable lesions, such as constrictive pericarditis, valvular disease or left ventricular aneurysm, should be referred for cardiological evaluation and the appropriate surgery. Patients with ischaemic induced heart failure should be assessed for possible revascularization by either angioplasty or bypass surgery. Together with clinical findings and cardiac diagnostic tests, appropriate therapy can be allocated accordingly (Figure 4).⁸⁴ ■

Figure 4: Management Algorithm of Heart Failure



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